

# Avian Testing

## *Dosing and Species Selection*



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# Avian Testing

## *Dosing and Species Selection*

### **Issues**

1. *Dosing study not conclusive in dosing scenario selection*
  - *No dose-response relationship*
  - *High aggression seen with Japanese quail - confounding factor?*
  - *Conflicting response between generations*
2. *Extensive list of endpoints evaluated in both the dosing study and the species selection*
  - *Endpoint Relevance*
  - *Use in risk assessment*
3. *Species selection for avian testing*

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## *Dosing and Species Selection*

### *Dosing study not conclusive in dosing scenario selection*

- *Lack of dose-response relationship*
  - *High variability in sex ratio*
  - *High variability in male sexual maturation*
  - *Histological response varied*
  - *Difficult to assess trend in plumage characteristics*
- *Japanese quail aggression*
  - *Strain, lighting, husbandry?*
- *Conflicting response between generations*
  - *Tibiotarsus/tarsometatarsus slightly increased in F1 males but decreased in F2*

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## *Dosing and Species Selection*

***Extensive list of endpoints evaluated in both the dosing study and the species selection***

- *Endpoint Relevance Must be Defined*
  - *Link Endpoint to Adverse Effect*
  - *Guideline Should Describe Relevance*
- *Use in Risk Assessment*
  - *Measurement versus Assessment Endpoint*
  - *Purpose to Protect Avian Populations (Apical Endpoints) or to Determine Mode of Action ?*

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## *Dosing and Species Selection*

### *Species selection for avian testing*

- *Few actual impacts from exposure to a known "estrogen"*
- *Bobwhite quail - 24 months/Japanese Quail - 10 months*
- *Similarity in response between species*
- *Delayed maturation and plumage possible endpoints - specifically endocrine?*

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### *Questions for Panel*

- *Statistics - acceptable, however, biological significance must be considered*
- *Preferred Dosing Scenario - inconclusive*
- *Draft Guideline - needs to clarify the purpose of the study, identify the relevance of endpoints and their use in decision-making*

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## *Dosing and Species Selection*

### ***Recommendations***

- *Dosing study*
  - *Additional work needed to identify best dosing scenario*
  - *Additional compounds - both positive and negative - needed to validate protocol and endpoints to be evaluated*
  - *Address equivocal responses: biological vs statistical significance - clarify data interpretation procedures*
- *Draft Guideline needs additional development*
  - *identify appropriate endpoints not just everything we can measure*
  - *Evaluate potential for husbandry/strain/logistics/resources to interfere with endpoint evaluation and success of study*
  - *Does a second generation add enough to justify resources, including animals?*